c.) Remarks

Office Action of May 4, 2006

Claims 1-4, 6, 8-9, 11-15, and 22 are pending. All pending claims stand rejected in the office action of May 4, 2006.

The following claim rejections are outstanding:

1) Rejection of claims 1-4, and 6 under 35 USC § 102(b) as anticipated by U.S. Patent 4,851,221 to Pak et al (hereinafter, "Pak") and as evidenced by the Merck Manual of Diagnosis and Therapy, 17th Ed., 1999 (hereinafter, "Merck Manual") and Bell et al., *Arch Intern Med* 1992: 152: pages 2441-2444 (hereinafter, "Bell").

2) Rejection of claims 8-9, 11-15, and 22 under 35 USC § 103(a)as being unpatentable over Pak in view of Merck Manual and further in view of Bell.

Each rejection is addressed below in turn.

1. Rejection of Claims 1-4, 6, 8-9, 11-15, and 22 under § 102(b)

Claims 1-4, 6, 8-9, 11-15, and 22 are rejected under § 102(b) as being anticipated by Pak. Although the examiner concedes that Pak does not expressly disclose the employment of calcium citrate compositions in increasing high-density lipoprotein levels (HDL) in plasma or the ratio of HDL to LDL in a postmenopausal women. The examiner also concedes that Pak does not expressly disclose that if the HDL level is increased, the administration is continued for at least about two months. The examiner then addresses the lack of the express teachings by using an inherency argument with support from the Merck Manual and Bell.

The examiner asserts that Pak discloses administration of a calcium supplemental composition comprising calcium citrate at a dose of 1 g (60 meq/day) or 1.5-2.75 g calcium/day to a postmenopausal woman for the treatment of various conditions such as hypoparathyroidism, osteoporosis, bone loss, hyperphosphatemia, and hypertension. The examiner asserts that Pak discloses a daily administration and that the calcium citrate composition of Pak is prepared from a pre-mix preparation with a calcium/citrate molar ratio of 1.25 of citric acid and a calcium compound such as calcium hydroxide. The examiner also asserts that Pak discloses the same effective amounts or doses of calcium citrate to be administered to the postmenopausal woman as instantly claimed.

The examiner then concedes that Pak does not disclose the employment of the calcium composition in methods of increasing HDL in plasma or ratio of HDL to LDL in a postmenopausal woman, and that Pak does not disclose that if HDL level in plasma is increased, the administration of the calcium composition should continue for at least about two months. Having recognized these deficiencies in the teachings of Pak, the examiner then dismisses them using an improper inherency argument. The examiner cites the Merck Manual for the proposition that the various conditions associated with postmenopausal women include hypercholesterol levels which require an increase in the HDL level or a lowering of the LDL level or increasing the ratio of HDL to LDL in said postmenopausal woman. Based upon, this, the examiner asserts that Pak's patient population encompasses or overlaps or is even the same as that population herein as needing an increase in HDL levels. For claims 2 and 3, the examiner states that the disclosure of Bell teaches that administration of calcium supplements would inherently increase an HDL level in plasma or a ratio of HDL to LDL in postmenopausal women

and that the increase would have been inherent by administration of calcium citrate in 1 g dose per day.

Applicants respectfully traverse this rejection. The fact that "cardiovascular diseases become more prevalent after menopause" provides no basis to assert that Pak's teachings inherently disclose the use of calcium supplementation for the treatment of hypercholoesterol levels. The argument of inherency is improper from a legal perspective and dubious from a scientific perspective. Pak makes no claims regarding effects, and therefore it does not make clear to whom one would give a calcium citrate supplement. Calcium is mainly prescribed to women for osteoporosis prevention - these subjects at risk of osteoporosis do not necessarily have a high HDL, and those with a high HDL are not necessarily at risk of osteoporosis. One could reasonably argue that men often have high HDL and are at low risk of osteoporosis (although the data in the instant application do not relate to men). The way the inherency argument is used by the examiner, it would seem to eliminate any possibility of specific claims regarding new uses of a composition that is already covered by a composition of matter patent (i.e., new uses of a known composition). This is clearly not the law and applicants assert that the rejection is not proper. Rejections based on inherency cannot be bottomed on mere possibilities; the mere fact that a certain thing *may* result from a given set of circumstances is not sufficient. *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981). In order to support a rejection based upon inherency, the result must necessarily be present in the prior art; it is not sufficient that it may likely be present in some instances, but not in others. Occasional results are not inherent. *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999). However, the examiner is basing his assertion of inherency precisely on probabilities. Pak gives no indication, and the examiner has no basis for assuming that anyone in the population of Pak had problems

with HDL levels or ratio of HDL:LDL and that administration of calcium citrate corrected such problem, if it existed. To presume such merely because "cardiovascular diseases become more prevalent after menopause" is mere speculation *based upon probability* (*i.e.*, "more prevalent"), which is precisely the type of reasoning that is forbidden by the relevant law of inherent anticipation.

While some postmenopausal women suffering from osteoporosis may also suffer from a high HDL, this is not necessarily so. A proper inherency rejection would require that it be necessarily so and that the treatment of Pak worked to correct the problem. There is no basis, outside of speculation based on probabilities, that Pak population covers those of the instant claims or that the method of Pak would treat the condition addressed in the instant claims. A teaching of the use of calcium supplementation for treatment of osteoporosis says nothing about the usefulness, or lack thereof, of using calcium supplementation for treatment of hypercholesterol levels or unhealthy HDL and LDL levels. Therefore, applicants assert that there is no teaching or suggestion in Pak (either expressly or inherently) to one of ordinary skill in the art that the employment of the calcium composition is useful in methods of increasing HDL in plasma or ratio of HDL to LDL in a postmenopausal woman, and that if HDL level in plasma is increased, the administration of the calcium composition should continue for at least about two months. This is true notwithstanding any and all of the teachings of Bell or Merck Manual. Pak does not disclose or suggest, either expressly, inherently, or otherwise, that the employment of the calcium composition is useful in methods of increasing HDL in plasma or ratio of *HDL* to *LDL* in a postmenopausal woman, and that if *HDL* level in plasma is increased, the administration of the calcium composition should continue for at least about two months. The Merck Manual is deficient as prior art in that it merely provides the unremarkable statement

that cardiovascular disease becomes more prevalent after menopause. It cannot be reasonably asserted that because a method is known to be beneficial in treating a certain condition that it is obviously beneficial in treating another condition, simply because the two conditions are more prevalent in older populations. The vast majority of medical conditions become more prevalent with advancing age. The secondary references of Merck Manual and Bell also fail to teach or suggest the administration of calcium citrate as claimed in the pending claims. As a result, the secondary references suffer from the same deficiency. Accordingly, the instant claims are patentable over Pak, the teachings of Merck Manual and Bell notwithstanding.

The examiner states that it is well known that calcium supplementation is used for postmenopausal women for treating various conditions. The examiner ignores that fact that what is not well known and what is not obvious, is that calcium supplementation is useful for postmenopausal women for treatment of unhealthy cholesterol, HDL, and LDL levels. What the instant invention teaches is that calcium supplementation is useful for postmenopausal women for treatment of unhealthy cholesterol, HDL and LDL levels, which is both novel and non-obvious over the cited references.

The examiner then asserts that although Pak does not expressly disclose measuring HDL levels in a postmenopausal woman, it would have been obvious to one of ordinary skill in the art in view of Pak to measure HDL levels when administering calcium citrate for increasing HDL levels. However, this statement disregards the fact that Pak does not teach or suggest the use of calcium supplementation for treatment of unhealthy HDL levels. It is unclear why the examiner feels it would be obvious to test a patient's cholesterol levels when one is trying to treat or prevent osteoporosis in the patient. Pak doesn't expressly disclose this for the very reason that Pak is not concerned with this.

The examiner states that "[n]ote that even the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable, or would not by itself carry patentable weight if the prior art teaches the same or nearly the same method steps." (citations omitted). However, the new use instantly claimed is NOT inherently present in the prior art and applicants respectfully assert that the examiner has used an incorrect legal standard for inherency; a standard based on probabilities. *See In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981); *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999).

The examiner is using extrinsic evidence (*i.e.*, the prior art of Merck Manual and Bell) to show inherency in Pak. The Federal Circuit in *Continental Can Co. U.S.A. v. Monsanto Co.*, 948 F.2d 1264, 1268-69 (Fed. Cir. 1991) has set out that:

> To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. **Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference,** and that it would be so recognized by persons of ordinary skill. . . .This modest flexibility in the rule that "anticipation" requires that every element of the claims appear in a single reference accommodates situations where the common knowledge of technologists is not recorded in the reference; that is, where technological facts are known to those in the field of the invention, albeit not known to judges. (emphasis added).

Applicants respectfully assert that the references of Merck Manual and Bell do not make clear that the missing descriptive matter is necessarily present in Pak. The fact that "cardiovascular diseases become more prevalent after menopause" provides no reasonable b0asis to conclude that the missing descriptive matter is necessarily present in Pak.

In light of applicant's arguments, applicants believe that the examiner's rejection under § 102(b) on a theory of inherent anticipation is improper in law in addition to being scientifically

and logically unpersuasive. Applicants respectfully request that the examiner withdraw the pending rejection and to allow the pending claims.

2. Rejection of Claims 8-9, 11-15, and 22 under § 103(a)

The examiner has rejected claims 8-9, 11-15, and 22 under 35 USC § 103(a) as being unpatentable over Pak in view of Merck Manual and further in view of Bell. The examiner states that Pak does not expressly disclose measuring the HDL level in a woman or the administration of calcium citrate for at least 6 months, and for at least 12 months as in claims 8., 9, and 15. The examiner then uses Bell to provide the teaching of the administration of a calcium supplement to women between the ages of 55 +9.3 years for 6 weeks to produce a 4.1% increase in HDL and a 4.4 % reduction in LDL, and further that when the calcium supplement was administered, a complete lipid profile is measured at weeks 0, 6, and 12.

Applicants respectfully traverse this rejection. The examiner cites Pak as discussed in the first rejection. This presumably includes the examiner's assertion that Pak inherently discloses the employment of calcium citrate compositions in increasing high-density lipoprotein levels (HDL) in plasma or the ratio of HDL to LDL in a postmenopausal women. As we indicated in the response to the first rejection, this is an improper rejection of anticipation inherency under § 102(b). Pak teaches the administration of calcium citrate for the treatment of various conditions such as hypoparathyroidism, osteoporosis, bone loss, hyperphosphatemia, and hypertension. Bell teaches the administration of calcium carbonate for treatment of hypercholesterolemia. Merck Manual is cited only for the proposition that that the various conditions associated with postmenopausal women include hypercholesterol levels which require an increase in the HDL level or a lowering of the LDL level or increasing the ratio of HDL to LDL in said postmenopausal woman.

As discussed above, Pak does not disclose the employment of calcium citrate compositions in increasing high-density lipoprotein levels (HDL) in plasma or the ratio of HDL to LDL in a postmenopausal women. The examiner's assertion of inherent anticipation under § 102(b) is improper as to both that law and the fact of what the supporting references actually disclose. Bell only teaches that calcium carbonate for treatment of hypercholesterolemia. None of Pak , Bell, or Merck Manual teaches the administration of calcium citrate to treat hypercholesterolemia. Because Pak and Bell are concerned with the treatment of distinctly different conditions, and there is no suggestion or motivation to combine the references, any combination of them does not teach the inventions of claims 8-9, 11-15, and 22. Furthermore, the examiner cites Merck manual for the proposition that the various conditions associated with postmenopausal women include hypercholesterol levels which require an increase in the HDL level or a lowering of the LDL level or increasing the ratio of HDL to LDL in said postmenopausal woman. This unremarkable statement of fact in no way teaches or suggests that use of calcium citrate for increasing HDL levels or increasing the HDL:LDL ratio in a post-menopausal women.

Accordingly, applicants respectfully assert that the combination of Pak in view of Merck Manual and further in view of Bell does not render claims 8-9, 11-15, and 22 unpatentable under § 103(a). Applicants respectfully request withdrawal of this rejection.

d.) Conclusions

In light of the arguments proved herein, applicants respectfully request withdrawal of the outstanding rejections and allowance of the pending claims. If any issues remain outstanding, please contact the undersigned for resolution of the same.

Applicants believe that no fees are associated with the filing of this response. However, if applicants are in error and any fees are owing, the Commissioner may charge Deposit Account No. 06-2375, under Order No. P02194US0/10104570, from which the undersigned is authorized to draw.

Respectfully submitted,

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By: _____

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